PIONEER
ACADEMIC PUBLISHING LIMITED

Current Research in Medical Sciences
ISSN 2958-0390
www.pioneerpublisher.com/crms
Volume 3 Number 2 June 2024

The Primary Nutritional Approach in Pediatric Cystic Fibrosis: A Mini-Review

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doi:10.56397/CRMS.2024.06.11

Abstract

In recent decades, diets for Pediatric Diseases have gained increasing acceptance, with disease-specific diets recommended in various international guidelines. This Mini-Review, a crucial resource for medical professionals, researchers, and students specializing in pediatric gastroenterology and nutrition, highlights the basic principles of diet in Cystic Fibrosis. The text will focus on primary dietary interventions that will benefit by removing, adding, supplementing, and restricting diets.

Keywords: dietary intervention, Cystic Fibrosis, malnutrition

Introduction

"Let food be thy medicine and medicine be thy food," the quotation credited to Hippocrates, holds a profound historical significance. It reminds us that since ancient Greek and Roman times, "disease" was used to denote physical imbalance, and food and diet have been considered crucial to restoring this imbalance. This historical context to understanding the evolution of diets for Pediatric Diseases has gained increasing acceptance in recent decades, with disease-specific diets now recommended in various international guidelines. Medical professionals, researchers, and students specializing in pediatric gastroenterology and nutrition are crucial in implementing these dietary interventions. This mini-review will explore the basic principles of the nutritional approach in cystic fibrosis, focusing on specific dietary interventions that will benefit from removing, adding, supplementing, and restricting diets.

Cystic Fibrosis (CF) is a severe, life-threatening multisystem disorder caused by variants of the Cystic Fibrosis Transmembrane Conductance Regulator (CFTR) gene. CFTR mutations disrupt fluid secretion, leading to viscous or acidic secretions, epithelial obstruction, and gastrointestinal symptoms. This disruption also thickens mucus secretions in the lungs, liver, pancreas, gallbladder, and intestines, causing stasis of intestinal contents and dysbiosis.

Cholestasis occurs due to increased bile viscosity, reduced bile acid concentration in small intestines, reduced delivery of digestive enzymes, and impaired critical nutrient absorption (Guo J, Garratt A & Hill A., 2022; Turck D, Braegger CP, Colombo C, Declercq D, Morton A, Pancheva R, et al., 2016; Mariotti Zani E, Grandinetti R, Cunico D, Torelli L, Fainardi V, Pisi G et al., 2023; Shteinberg M, Haq IJ, Polineni D & Davies JC., 2021).

Malnutrition and CF

CF, the most common life-shortening genetic disorder, significantly impacts the patient's nutritional status, primarily due to pancreatic insufficiency (Guo J, Garratt A & Hill A., 2022; Mariotti Zani E, Grandinetti R, Cunico D, Torelli L, Fainardi V, Pisi G et al., 2023; Li L & Somerset S., 2014). This prevalence of malnutrition in CF is a stark reality that individuals affected by CF and their caregivers must confront. It is a condition that demands immediate attention and comprehensive understanding. Table 1 provides a comprehensive overview of the reasons and consequences of Undernutrition in CF.

Table 1. Undernutrition in Cystic Fibrosis: reasons and consequences

Persistent lung inflammation
Enteric intestinal inflammation
Insufficient release of pancreatic enzymes; Low bicarbonate output
Bacterial Overgrowth in small intestinal
CF-related liver disease (Impaired liver function)
Endocrine Pancreatic Insufficiency (CF-related diabetes)
Immunological impairment and Infections associated
High energy requirements; decreased appetite and oral intake relative to needs
Insufficient and inadequate Nutrient Intake
Malabsorption and energy losses
Substantial Energy Expenditure
Higher Essential Fatty Acid Turnover
Poor nutritional status, low weight- and height-for-age percentiles
Psychosocial issues (stress and treatment noncompliance)
Worsen pulmonary status, impaired growth, lower quality of life, impaired cognitive function, and shorten life expectancy

Clinical Assessment, Nutritional Status, and Diet History

A complete and thorough physical exam, a cornerstone of each clinical visit, is crucial in providing numerous clues to the nutritional status, and evidence of nutritional deficiencies emphasizes the vital role of healthcare professionals in patient care. Rest assured, a comprehensive diet history is also necessary to assess eating patterns, nutrients, and caloric intake. Inquiring about adverse eating behaviors such as pain or difficulty swallowing, coughing or choking with eating, abdominal pain or vomiting after eating, early satiety, and constipation can offer additional insight into factors contributing to poor caloric intake. Obtaining a 'usual' daily intake or a '24-hour recall' may suffice for a well-nourished individual who is gaining weight appropriately and enjoys most foods.

Macronutrients in CF

When it comes to macronutrients, many individuals with CF will likely require higher nutrient intakes to overcome stool losses, which refers to the excessive loss of nutrients through the stool and achieve expected growth or weight gain/maintenance. However, the specific needs will depend on the severity of the illness. For a detailed breakdown, please refer to Table 2.

Table 2. Macronutrients recommendation (Compiled from references 2 and 5)

Energy intake	All ages: 110%-200% of energy requirements for same-age healthy children/adolescent
Protein	20% of the total caloric intake
Fat	35-40% of the total caloric intake
Carbohydrates	40-45% of the total caloric intake
Dietary Fiber	Age plus 5 g

Energy and Protein Recommendations

Adhering to dietary guidelines is crucial for CF

patients, who require more calories than the average population. The recommended daily allowance (RDA) for energy allows for average growth for age by compensating for malabsorption and increased calorie needs secondary to pulmonary dysfunction and any required catch-up growth. The European guidelines recommend that energy intake range from 120–150% in terms of the energy requirements of a healthy population. On the other hand, US guidelines recommend 110% to 200% (Mariotti Zani E, Grandinetti R, Cunico D, Torelli L, Fainardi V, Pisi G et al., 2023). Current consensus guidelines recommend that children with CF consume 35-40% of their caloric intake from fat, 20% from protein, and 40-45% from carbohydrates (Wilschanski M, Braegger CP, Colombo C, Declercq D, Morton A, Pancheva R, et al., 2016; Schindler T, Michel S & Wilson AW., 2015) (Table 2). Some factors that may reduce caloric intake include poor appetite, doses or adherence to the PERT administration, the need for PPI therapy, Gastroesophageal Reflux Disease, and Constipation.

Fat

Patients with high energy needs may benefit from a diet higher in fat (approximately 35% of total calories). With adequate enzyme intake, no clear benefit of medium-chain fats or hydrolyzed proteins has been found compared to long-chain fats. Initial recommendations for a high-fat diet were to aim for a fat consumption of 35–45% of total calories. A high-fat, high-calorie diet has been the usual care for CF because of its effect on pulmonary function and survival.

• Cardiovascular health may be affected by a diet high in saturated fat.

• A diet high in fat may be a source of increased oxidative stress. The increase in plasma fatty acids correlated with an increase in oxidative stress, further complicated by a lack of observed improvement in antioxidant circulation. So, due to concern about the ongoing oxidative stress, it has been suggested that patients with CF may benefit from a diet rich in antioxidants to help optimize the benefits of a high-fat diet.

• Due to malabsorption, children and adolescents must receive a high-calorie, high-fat, vitamin supplementation and pancreatic enzyme (Wilschanski M, Braegger CP, Colombo C, Declercq D, Morton A, Pancheva R, et al., 2016; Schindler T, Michel S & Wilson AW., 2015).

Protein

Protein is an essential nutrient to prevent catabolism; recommended intakes are 1.5–2 times greater than the recommended daily allowance or ~15% of total calories. Each gram of protein provides four calories, so protein is not as efficient an energy source as fat. However, adequate protein intake is critical to maintaining bodily structures and providing the essential amino acids. In order to be absorbed in the intestine, proteins must be denatured by stomach acid and then broken down into di- and tri-peptides and free amino acids. The average dietary intake of protein is 10–15% of total kcal. Protein requirements for individuals with CF have been expressed differently; however, overall agreement is that the CF diet should be high in protein. An increase of 1.5–2 times above the RDA for age has been recommended. According to ESPEN-ESPGHAN-ECFS, a protein intake of 1.5 g/kg/day is recommended and adjusted based on the levels of pre-albumin and C-reactive protein (Turck D, Braegger CP, Colombo C, Declercq D, Morton A, Pancheva R, et al., 2016; Wilschanski M, Braegger CP, Colombo C, Declercq D, Morton A, Pancheva R, et al., 2016).

• In the general population, a diet exceptionally high in protein can put an individual at risk for azotemia, metabolic acidosis, and neurodevelopmental problems. These effects have been observed in patients consuming 4–6 g of protein per kilogram of body weight.

• Individuals with renal or liver disease are particularly at risk for the toxic effects due to limitations in metabolizing and excreting protein.

• Protein is essential to prevent catabolism. Protein requirements for individuals with CF must be 1.5–2 times above the RDA for age-recommended intakes or ~15% of total calories. However, a diet exceptionally high in protein can put an individual at risk for azotemia, metabolic acidosis, and neurodevelopmental problems (Wilschanski M, Braegger CP, Colombo C, Declercq D, Morton A, Pancheva R, et al., 2016; Schindler T, Michel S & Wilson AW., 2015).

Carbohydrates

There are no specific recommendations for carbohydrate provision and intake, which is generally adequate in people with CF. The general population is recommended to get

45–65% of total energy from carbohydrates. The carbohydrate digestion begins with salivary amylase and is completed with pancreatic amylases and brush border enzymes. Unlike fat and protein, individuals with CF have been observed to have minimal loss of carbohydrates in their stool. Carbohydrate loss has been observed to be less than 1% of consumed carbohydrates in patients on standard PERT compared to the loss of approximately 40% of consumed fat and 20% of consumed protein (Turck D, Braegger CP, Colombo C, Declercq D, Morton A, Pancheva R, et al., 2016; Li L & Somerset S., 2014).

• A high carbohydrate intake has been associated with increased carbon dioxide production, which could exacerbate respiratory status, especially in particularly sick individuals.

• With the increasing occurrence of CF-related diabetes in the aging CF population, glucose tolerance has become a concern.

• Formulas high in carbohydrates were found to increase serum glucose concentrations and thus exacerbate hyperglycemia significantly.

Dietary Fiber

Dietary fiber's main physiological effect is on the colon, and its subsequent impact on health depends on its solubility, fermentability, viscosity, and gel-forming ability. So, in the colon, it increases stools' bulk and laxative properties, stimulates colonic fermentation, and enhances transit time (Dai FJ & Chau CF., 2017; Augustin LSA, Aas AM, Astrup A, Atkinson FS, Baer-Sinnott S, Barclay AW, et al., 2020).

There needs to be a consensus on the appropriate Dietary Fiber for individuals with CF. High fiber intake may cause calorie displacement and possibly abdominal pain exacerbations. Generally, a high-fiber diet is recommended for bowel health, cardiovascular health, and cancer prevention. Due to the focus on a high-calorie diet, a high-fiber diet still needs to be promoted in CF patients. Fibers are not digestible and, as such, provide minimal calories. The bacteria in the colon can convert some fiber to short-chain fatty acids (SFCA), which are essential fuel for colonocytes; this conversion allows fiber to contribute up to 1.5–2.5 cal/g. **It may be wise to recommend that patients incorporate** fiber-rich foods, mainly fruits, vegetables, legumes, and whole grains, providing the additional benefit of being rich in vitamins, minerals, and antioxidants (Wilschanski M, Braegger CP, Colombo C, Declercq D, Morton A, Pancheva R, et al., 2016).

Vitamins, Minerals, Electrolytes, and Trace Elements (Table 3)

A child with CF may have insufficient levels of fat-soluble vitamins due to the malabsorption caused by exocrine pancreatic insufficiency, poor nutritional intake, and changes in metabolism. In patients with pancreatic insufficiency, evaluating plasma levels of fat-soluble vitamins after initiating enzyme supplementation is adequate. Vitamins should be taken with high-fat food and pancreatic enzyme supplements to improve absorption (Cystic Fibrosis Foundation; Borowitz D, Robinson KA, Rosenfeld M, Davis SD, Sabadosa KA, Spear SL, et al., 2009; Rana M, Wong-See D, Katz T, Gaskin K, Whitehead B, Jaffe A, et al., 2014).

Rest assured, the suggested nutritional interventions for CF are effective. CF may have higher than standard salt, calcium, iron, zinc, and selenium requirements due to increased sweating, intestinal malabsorption, and chronic inflammation. The risk for sodium loss is frequent in CF, such as in hot environmental conditions, fever, breathing, fluid loss due to diarrhea, and vomiting. Additionally, the sodium content of breast milk and standard infant formula is relatively low (<7 mmol/L in breast milk and <15 mmol/L in formula). Additionally, most first-baby foods have low sodium content (Sermet-Gaudelus I, Mayell SJ & Southern KW., 2010; Sermet-Gaudelus I, Bianchi ML, Garabédian M, Aris RM, Morton A, Hardin DS, et al., 2011).

Zinc deficiency is related to anorexia, delayed growth, susceptibility to infections, delayed sexual maturation, and eye problems. Calcium must be supplied in CF due to a vitamin D deficiency (a fat-soluble vitamin) and a low dietary calcium intake. Iron deficiency is common in people with CF, and multiple factors can contribute, including malabsorption, chronic infection and inflammation, chronic blood loss, and inadequate intake (Sermet-Gaudelus I, Bianchi ML, Garabédian M, Aris RM, Morton A, Hardin DS, et al., 2011).

Table 3. Vitamins, Minerals, Electrolytes, and Trace Elements (Compiled from references 2 and 6)

	Assess	Recommendation
Vitamin A	Monitor annually and 3-6 months after a dosage change	Provitamin A (beta-carotene) If low serum values: 1 mg/kg/day (maximum 50 mg/day) for 12 weeks Maintenance dose: maximum 10 mg/day
Vitamin D	Monitor annually and 3-6 months after a dosage change	Vitamin D3 (cholecalciferol) Infants: 400 IU/day (upper limit of 1000 IU/day) All others: 800 IU/day 1-10 years: upper limit of 2000 IU/day Older: upper limit 4000 IU/day
Vitamin E	Monitor annually and 3-6 months after a dosage change	α-Tocopherol Infants: 50 IU/day Older children and adults: 100-400 IU/day
Vitamin K	Monitor annually by INR	Vitamin K1 Infants: 0.3-1.0 mg/day Older children and adults: 1-10 mg/day
Vitamin B12		Supplement after extensive ileal resection or Deficient: 100 mg/mo, intramuscular
Vitamin C	Nutritional intake assessed annually	If insufficient intake: Infants: 0.3-1.0 mg/day Older children and adults: 1-10 mg/day
Folic acid		Women planning to become pregnant, and during the first trimester of pregnancy: 400 mg/day.
Calcium	Calcium intake assessed annually	0-6 months: 200 mg 7-11 months: 280 mg 1-3 years: 450 mg 4-10 years: 800 mg 11-17 years: 1150 mg 18-25 years: 1000 mg
Iron	Monitor serum iron annually	If iron deficiency occurs, first resolve underlying inflammation, and supplement if deficiency persists
Sodium	Hot weather Fluid Loss: Vomiting, Fever, Diarrhea, Tachypnea, Ostomies, Stress Situations (exercise/sports, hot), Excessive Sweating	Breastfed infants 0-6 months: 1-2 mmol/kg/day All Infants: up to 4 mmol/Kg/day Older Children and Adolescents: Salty foods or sodium chloride capsules Salt (sodium chloride) should be given in small portions throughout the day, diluted in water or formula.
Zinc	Growth retardation, susceptibility to infections, delayed sexual maturation	Supplement if risk: < 2 years: 1 mg /kg/day (max 15 mg/day) for six months 2-18 years: 15 mg/day for six months
Selenium		No routine supplementation is recommended.

Note: 1 mcg retinol = 3.33 IU vitamin A = 24 mcg alfa-carotene. 1 μg cholecalciferol = 40 IU vitamin D. 1 mg alfa-Tocopherol = 1.5 IU vitamin E. INR = International Normalized Ratio, prothrombin time (PT).

Nutrition Intervention

CF patients require a balanced intake of essential nutrients, including proteins, fats, carbohydrates, vitamins, and minerals. The detrimental effects of nutrient deficiencies in infants, children, and adults with CF underscore the necessity for early and aggressive nutrition intervention, commencing in the first years of life and persisting throughout the lifespan. Similarly, research indicates that increased consumption of Essential Fatty Acids (EFAs), such as linoleic acid, can enhance survival and growth. Diligent care involving aggressive pulmonary interventions and appropriate nutrition has been linked to extended survival rates. A history of poor nutritional status has consistently correlated with unfavorable clinical outcomes in CF patients. It is evident that meticulous attention to care, including aggressive pulmonary interventions and appropriate nutrition, can lead to prolonged survival—interventions to enhance nutritional status, such as supplemental feeding (enteral and parenteral).

The nutritional management of CF begins with a crucial step in determining pancreatic insufficiency. This responsibility lies with healthcare professionals, who play a pivotal role in immediately improving supplemental feeding (enteral and parenteral), increasing calories, and positively impacting nutritional and respiratory status. People with CF diagnosed early through newborn screening programs benefit from earlier intervention, allowing for minimizing nutritional deficits (Leonard A, Bailey J, Bruce A, Jia S, Stein A, Fulton J, et al., 2023).

In summary, a child with CF needs: (Turck D, Braegger CP, Colombo C, Declercq D, Morton A, Pancheva R, et al., 2016; Wilschanski M, Braegger CP, Colombo C, Declercq D, Morton A, Pancheva R, et al., 2016; Stallings VA, Stark LJ, Robinson KA, Feranchak AP & Quinton H., 2008).

• Nutritional support for children younger than two years of age: a weight-for-length percentile > the 50th is recommended. For children from two to 18, the BMI may be assessed, and the nutritional status is recommended, maintaining a BMI percentile > 50. A high-calorie, high-fat diet and supplementation of fat-soluble vitamins in conjunction with control of malabsorption with pancreatic enzyme replacement is hugely recommended.

• The high-calorie diet improves nutritional status, prolonging survival. High-fat foods will help achieve high-calorie needs, but encouraging intake of mono- and polyunsaturated fatty acids may help prevent cardiovascular complications in a population experiencing increasing longevity.

• Although there are no specific recommendations regarding the type of fat to prevent essential fatty acid deficiency, a diet containing adequate energy, balanced intake of polyunsaturated fatty acids (n-6 and n-3), and antioxidants are indicated. Vegetable oils such as canola, soy, and cold-water marine fish are good sources of linolenic acid and energy.

• Guidelines recommend adjusting energy intake to avoid obesity.

• In addition, an increased protein intake maintains lean body mass and improves long-term outcomes.

• Appetite stimulants can be an adjuvant to other interventions and have been proven to provide nutrition-related advantages with a reasonably safe side effect profile.

• The goals of nutritional support in patients with pulmonary disease include adequate caloric intake, protein intake, correction of respiratory failure (reversal of the nutritional-related sequelae of lung disease), avoidance of excess carbon dioxide production, and optimization of exercise.

The Nutrition Supports

The goal is to begin as early as possible after diagnosis, including achieving an optimal nutritional status to support the growth stages and puberty development in children and further supporting the maintenance of an optimal nutritional status in adult life.

• **Children < two years**. Percentiles of weight and height should be used to evaluate growth, and a weight-for-length percentile equal to or greater than the 50th percentile is recommended.

• **For children two to 18 years**, nutritional status may be assessed by BMI, which recommends attaining and maintaining a BMI percentile equal to or greater than 50 (Turck D, Braegger CP, Colombo C, Declercq D, Morton A, Pancheva R, et al., 2016; Stallings VA, Stark LJ, Robinson KA, Feranchak AP & Quinton H., 2008).

Feeding Methods

According to ESPEN/ESPGHAN guidelines (Turck D, Braegger CP, Colombo C, Declercq D, Morton A, Pancheva R, et al., 2016), nutritional support with diet modification and oral nutritional supplementation could be initiated in children under two, and the weight-for-length between the 10th and 50th percentile. In those between 2 and 18 years old, the intensification of the nutritional support is required in case of BMI percentile between the 10th and 50th percentile, weight loss, or no weight gain in the last two months.

Oral Nutritional Supplementation

In clinical practice, Oral Supplementation should be considered by eating more or more often, fortifying food (i.e., adding extra oil or fat), and consuming more calorie-dense foods. High-energy-dense formulations should be given, usually before meals or bedtime. CF dietitians can advise on foods that can enhance weight gain, including adding linoleic-rich vegetable oils, butter, oil, cheese, and cream to foods. Encouraging small frequent meals and snacks can also help. Linoleic acid supplementation may reduce the need for general high-energy supplements.

Enteral Feeding

When the oral caloric intake is insufficient to reach the anthropometric nutritional goals, enteral feeding should be initiated. There are various devices and formulas for feeding enterically. The patient's clinical status determines the approach. Enteral nutrition can be administered by a nasogastric tube and is recommended for short-term duration (<3 months) to avoid complications (tube dislodgement, nasal bleeding or erosion, and intestinal perforation). However, gastrostomy tubes are the most frequently used, especially for long-term enteral feeding. Feeds may be administered as a bolus during the day or continuously overnight. If co-morbidities, such as gastroesophageal reflux disease, gastroparesis, or pancreatitis, the enteral feeds should be introduced via jejunal or gastro-jejunal tubes. Continuous infusions are required (Conway, S., Morton, A., & Wolfe, S., 2012).

There has yet to be a consensus regarding using a specific type of formula (polymeric, semi-elemental, elemental). The polymeric formulas are usually iso-osmotic and contain whole proteins, oligo- or polysaccharides, and medium- or long-chain triglycerides. Polymeric formula with a high energy (1.5 to 2 Kcal/mL) is first administered in most patients. On the other hand, elemental formulas contain small peptides or amino acids, the lipid content is minimal and is hyper-osmotic. Semi elemental formulas are between elemental and polymeric formulas. It is suggested that isotonic formulas are better tolerated than hypertonic formulas.

Parenteral Nutrition

Parenteral nutrition is not routinely advised in patients with CF and, if necessary, is not recommended for the long term due to the high risk of infection, associated liver disease, central access, and the high cost. Nevertheless, in case of contraindications for enteral nutrition, it could be helpful in intestinal resection (short bowel syndrome), meconium ileus, intestinal failure, and patients enlisted for transplant (Turck D, Braegger CP, Colombo C, Declercq D, Morton A, Pancheva R, et al., 2016; Wilschanski M, Braegger CP, Colombo C, Declercq D, Morton A, Pancheva R, et al., 2016; Sinaasappel M, Stern M, Littlewood J, Wolfe S, Steinkamp G, Heijerman HG, et al., 2002).

Special Considerations

The diagnosis of CF often occurs during the first couple of weeks of life when breastfeeding is becoming established. The stress of diagnosis and additional infant care requirements could contribute to a rapid decline in breastfeeding in infants with CF. Nourishing the infant with CF through the first years of life is of utmost importance. Moreover, a team approach is required to optimize the infant's overall health. Approximately 85% of patients with CF present with pancreatic insufficiency,

• Usually starting shortly after birth

• A comprehensive yet individualized nutrition plan for the infant newly diagnosed with CF often includes initiating pancreatic enzymes, fat-soluble vitamins, salt supplementation, breast milk, infant formula, and complementary foods.

• Table 4 focuses on primary dietary interventions that will benefit by removing, adding, supplementing, and restricting diets.

Table 4. Summary of nutritional treatment for Cystic Fibrosis in Pediatrics: removing, adding, supplementing, and restricting in dietary management

	Dietary Management				
	Removing	**Adding**	**Supplementing**	**Restricting**	**Reintroducing**
Cystic Fibrosis (CF)	Removing food or nutrients should be done individually and with caution.	The caloric requirement is higher than normal recommendations for a high-fat diet. Protein intake should be higher than that of the general population, foods containing calcium, iron, vitamin C, and antioxidants should be considered.	Supplemental formula is recommended for insufficient intake. Micronutrient supplementation, especially fat-soluble vitamins, calcium, and iron. Supplementation with medium-chain triglycerides can be carried out in cases of malabsorption.	Restriction of a diet high in saturated fat.	Not especially recommended

Pancreatic Enzyme Replacement Therapy (PERT)

Nutrition is the basis of CF treatment. Indeed, pancreatic insufficiency decreases fat absorption (even with PERT) and reduces nutrient intake; thus, understanding optimal PERT, using supplements, and knowing about deficiencies can help improve overall care for pancreatic insufficiency. The diagnosis of pancreatic insufficiency within the first year of life is typically by fecal elastase (Caras S, Boyd D, Zipfel L & Sander-Struckmeier S., 2011; Lahiri T, Hempstead SE, Brady C, Cannon CL, Clark K, Condren ME, et al., 2016; Barben J, Rueegg CS, Jurca M, Spalinger J, Kuehni CE & Swiss Cystic Fibrosis Screening Group, 2016).

Consensus guidelines recommend that PERT be initiated at a dose of 2000–5000 lipase units at each feeding, adjusting the dose of no greater than 2500 lipase units per kg per feeding. The maximum daily dose must be 10,000 lipase Units/ kg/day to reduce the risk of fibrosing colonopathy (Borowitz DS, Grand RJ & Durie PR., 1995; Schwarzenberg SJ, Wielinski CL, Shamieh I, Carpenter BL, Jessurun J, Weisdorf SA, et al., 1995; Borowitz D, Gelfond D, Maguiness K, Heubi JE & Ramsey B., 2013). Table 05 displays the basis of PERT. The addition of proton pump inhibitors may improve the efficiency of PERT.

Table 5. Pancreatic Enzyme Lipase Replacement Therapy (PERT) according to references (Turck D, Braegger CP, Colombo C, Declercq D, Morton A, Pancheva R, et al., 2016; Wilschanski M, Braegger CP, Colombo C, Declercq D, Morton A, Pancheva R, et al., 2016)

Age	Supplementation	
Up to 12 months	2000-4000 U lipase/120 mL • formula or • estimated breast milk intake • approximately 2000 U lipase/gram dietary fat in food	Orally as enteric-coated tablets or microspheres administered orally at the beginning of the feeding, and effective for about 45 minutes. Enzyme capsules should be

		opened, and the contents should be mixed with small amounts of applesauce.
1-4 years	2000-4000 U lipase/gram dietary fat. • Increasing dose upward as needed. • maximum dose 10,000 U lipase/kg per day)	Monitoring to determine the adequacy of PERT • every clinic visit for infants. • Every three months for older children and adolescents
Children >4 years	Starting at 500 U lipase/kg/meal, titrating • 1000-2500 U lipase/kg per meal, or • 10,000 U lipase/kg per day, or • 2000-4000 U lipase/gram dietary fat taken with all fat-containing meals, snacks, and drinks	PERT is vital to maintaining adequate nutritional status.

Breastfeeding

• Strategies to promote breastfeeding include lactation support services, emotional support during the time of diagnosis, and encouragement to seek help for the caregivers of newly diagnosed infants with CF from extended family and friends. Clinicians may be concerned with meeting the energy requirements of infants with CF who breastfeed. Human milk is the initial feeding type for infants with CF. The benefits of feeding human milk to healthy infants are well recognized. Reduction in respiratory and diarrheal infections, the risk for sudden infant death syndrome, better neurodevelopment, prevention or delay of atopic dermatitis, cow milk allergy, wheezing in early childhood, and enhanced maternal-infant bonding, among others, are well documented.

• Fortified breast milk and formulas ranging from 22 to 30 cal/oz (73–100 cal/100 mL) can be used to promote catch-up weight gain, meet increased energy expenditure related to illness, and provide concentrated calories if the infant is only able to consume a limited volume of breast milk or formula. Calorie concentration can be achieved by adding powdered infant formula to standard formula or breast milk.

• Despite the known benefits of breastfeeding, infants with CF are more likely to receive formula compared to breast milk. Cow milk-based formulas are recommended when formula feeding is used for infants with CF. Although breastfeeding should be encouraged for all infants with CF, parental choice should be considered, and all mothers should be supported in their decision to breastfeed or not.

• If infants are fed formula, standard infant formulas (as opposed to hydrolyzed protein formulas) should be used. Calorie-dense feedings should be used if there is inadequate weight gain or weight loss.

• At about six months, solids should be introduced at the same age as recommended for the non-CF population. Complementary foods should be introduced to infants with CF. Higher-calorie food choices should be emphasized, particularly for infants with poor weight gain. Adding fat to infant foods and selecting food sources that contain higher amounts of calories are all strategies to maximize the calorie intake of solid foods and promote average growth rates in infants with CF.

Education

Factors associated with dietary adherence, bothersome child mealtime behavior, and unsuccessful parenting strategies are predictors of lower calorie intake and weight status. Education, behavioral counseling, and help parents know what to expect as the child ages and when more intensive intervention may be necessary. Guarantee that qualified team members and family know the nutrition assessment—anticipatory guidance about developmental behavior. Deliver messages to families by all team members regarding the importance of nutrition, and nowadays, introduce all components related to preventing the development of overweight and obesity (Bailey J, Krick S & Fontaine KR., 2022; Gabel ME, Fox CK, Grimes RA, Lowman JD, McDonald CM, Stallings VA, et al., 2022).

Conclusions

CF is a severe, life-threatening multisystem disease with a high prevalence of malnutrition. Individuals affected by CF and their caregivers must face a harsh reality daily resulting from countless care tasks. Maintaining nutritional status, with high vigilance to avoid nutritional deficiencies, is the basis of therapy associated with pancreatic enzyme replacement therapy. So, adhering to dietary guidelines is crucial for CF patients to be healthy. In CF, nutrition support should begin as early as possible after diagnosis. The nutritional status achieving the growth stages and puberty development will further support an optimal nutritional status in adult life.

Conflict of Interest

The authors have no conflicts of interest.

Funding Statement

The authors declare no financial funding.

Author Contributions

Bibliographical Survey (NCM, JTD, GNH, TKW, MAC), drafting of the manuscript (TKW, NCM, MAC), critical manuscript revision (NCM, TKW, CDFJ).

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